

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1-63. (Canceled)

64. (Previously presented) A method for identifying a covalent modification of an amino acid residue in a polypeptide chain comprising:

detecting a mass difference between a formed polypeptide and a modified polypeptide by mass spectrometry, wherein the modified polypeptide comprises a covalent modification of an amino acid residue in the formed polypeptide, whereby the mass difference identifies the covalent modification.

65. (Previously presented) The method of claim 64 wherein the covalent modification is phosphorylation.

66. (Previously presented) The method of claim 64 wherein the covalent modification is acetylation.

67. (Previously presented) The method of claim 64 wherein the covalent modification is glycosylation.

68. (Previously presented) The method of claim 64 wherein the covalent modification is a disulfide bond.

69. (Previously presented) The method of claim 64, wherein said mass spectrometry is ion trap mass spectrometry.

70. (Previously presented) The method of claim 64, wherein said mass spectrometry is quadripole mass spectrometry.

71. (Previously presented) The method of claim 64 further comprising:

- (i) producing reaction mixtures from the formed and the modified polypeptide, each reaction mixture containing a peptide ladder comprising a series of adjacent polypeptides in which each member of the series differs from the next adjacent member by one amino acid residue;
- (ii) determining the differences in molecular mass between adjacent members of each series by mass spectroscopy, said differences coupled with the positions of said adjacent members in the respective series being indicative of the identity and position of the amino acid residue in the formed or modified polypeptide;
- (iii) identifying an amino acid residue in the modified polypeptide that comprises a covalent modification wherein the amino acid residue is identified by having an additional mass difference compared with the corresponding amino acid residue in the formed polypeptide.

72. (Previously presented) The method of claim 71 wherein producing the peptide ladders comprises:

- (1) reacting the formed and modified polypeptide with a molar excess of a pair of reagents comprising a coupling reagent and a terminating reagent each of which forms a reaction product with a terminal amino acid residue of the formed or modified polypeptide to be analyzed under a first reaction condition; the reaction product generated between the terminating reagent and the terminal amino acid residue of the formed or modified polypeptide being stable under all subsequent reaction conditions; the reaction product generated between the coupling reagent and terminal amino acid residue of the polypeptide to be analyzed being removable as a cleavage product from the original formed or modified polypeptide under a second reaction condition;

(2) changing the reaction conditions so that the cleavage product separates, thereby to form a reaction mixture comprising:

- i. unreacted coupling and terminating reagents,
- ii. a first reaction product which is the reaction product between the original formed or modified polypeptide and the terminating reagent,
- iii. a newly formed polypeptide from which the terminal amino acid residue has been removed;

(3) repeating steps (1) and (2) any selected number of cycles thereby to form a final mixture which comprises:

- i. reaction product between the original formed or modified polypeptide and the terminating reagent,
- ii. a peptide ladder which is series of adjacent reaction products which is formed by reaction between the terminating reagent and the terminal amino acid residue of a fraction of the newly generated polypeptide of each cycle, and

(4) determining the differences in molecular mass between adjacent members of the series of reaction products by mass spectroscopy, said differences being equal to the molecular mass of the amino acid residue cleaved from the original formed or modified polypeptide and from each subsequent formed or modified polypeptide of the series, said differences coupled with the positions of said adjacent members in the mass spectrum being indicative of the identity and position of that amino acid residue in the original formed or modified polypeptide.

73. (Currently amended) The method of claim 72 wherein the coupling agent reagent is PITC, the terminating agent reagent is PIC, the first set of reaction conditions comprises basic conditions and the second set of conditions comprises acidic conditions.

74. (Previously presented) The method of any of claims 64, 65, 66, 67, 68, 69, 70, 71, 72, or 73 wherein the formed polypeptide and the modified polypeptide are analyzed simultaneously in a mixture.